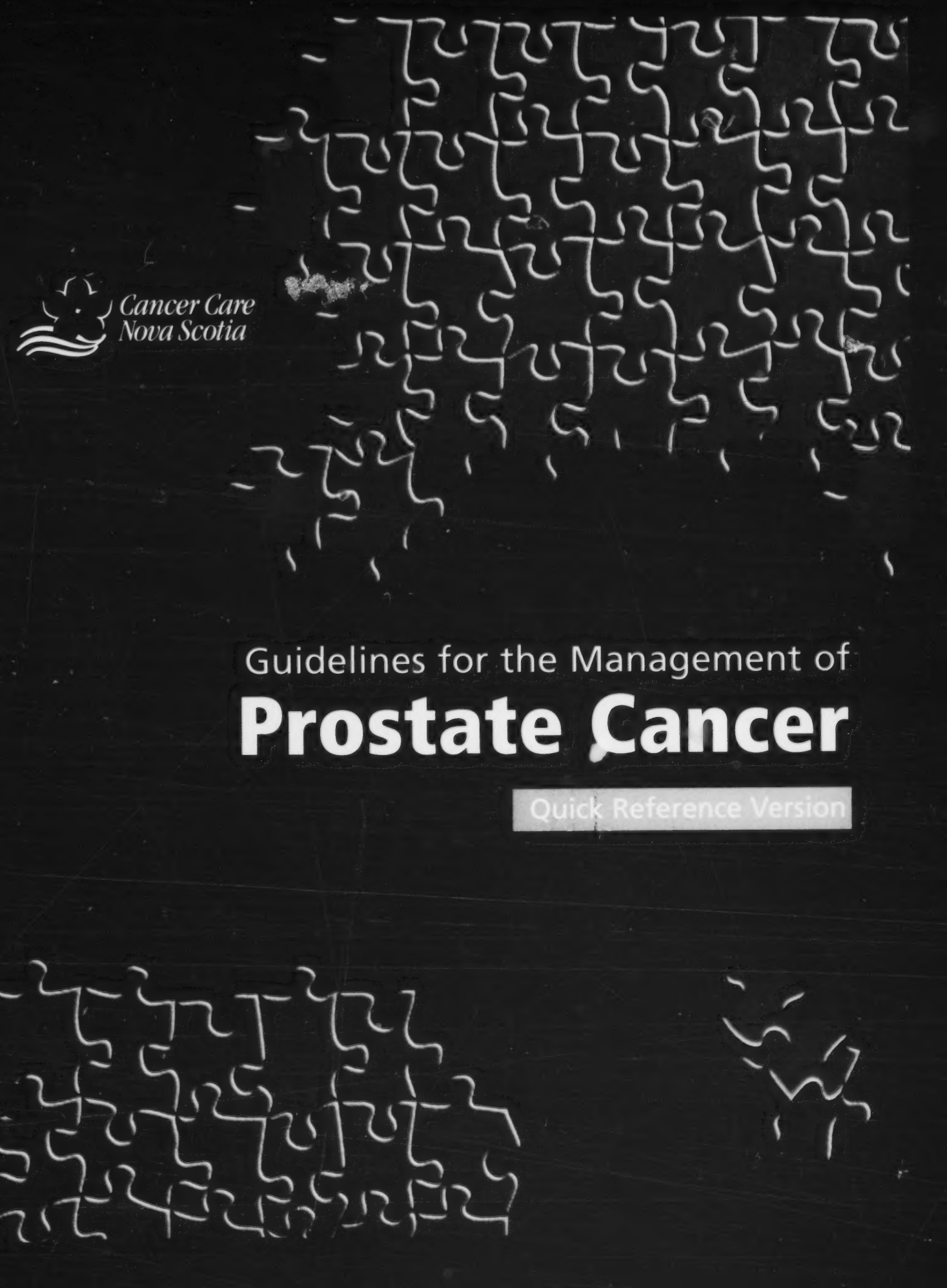

Cancer Care
Nova Scotia

Guidelines for the Management of

Prostate Cancer

Quick Reference Version

106-04048/

Cancer Care
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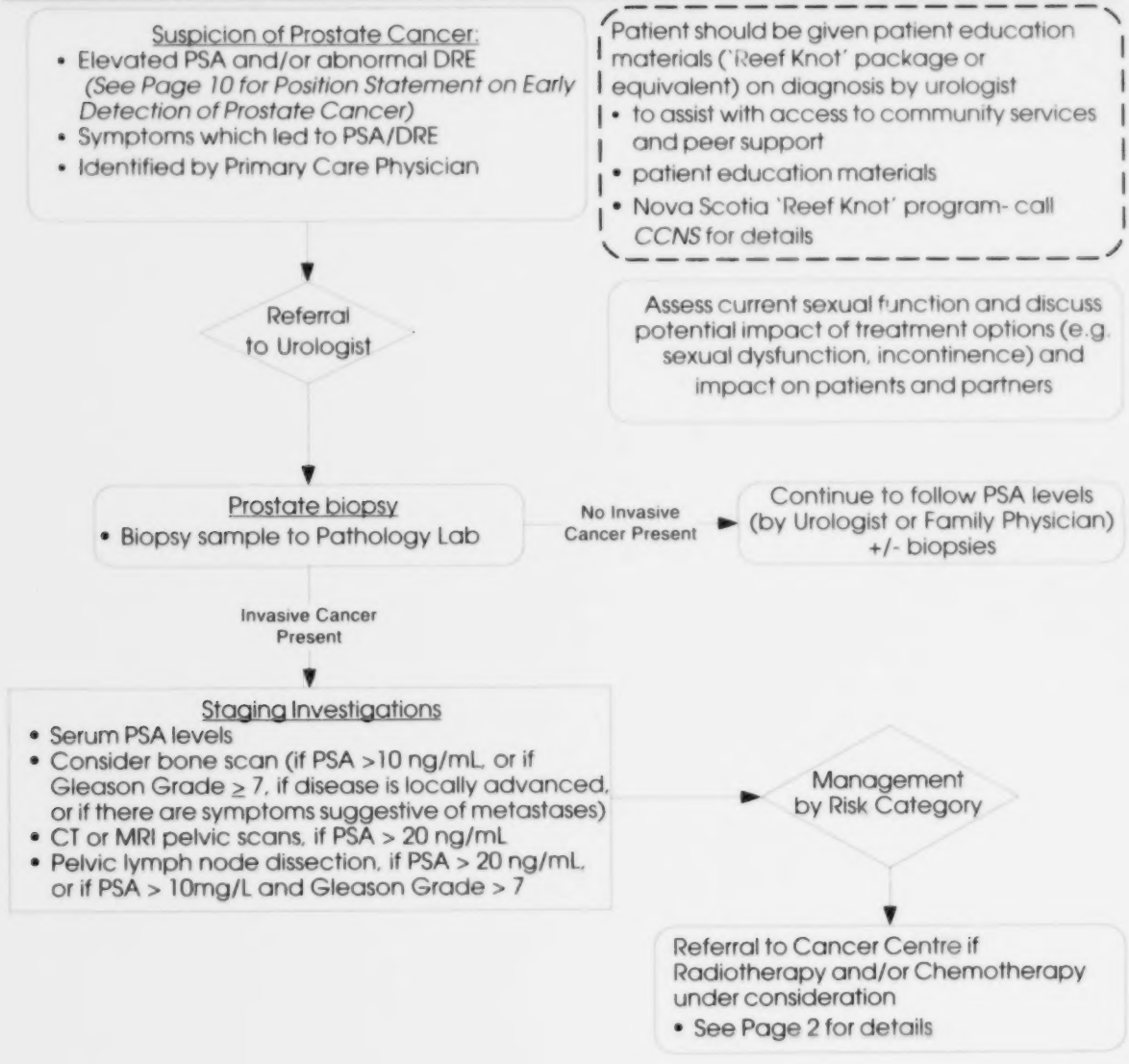
Quick Reference Version

Diagnosis and Referral of Prostate Cancer- Overview


Suspicion of Prostate Cancer:
• Elevated PSA and/or abnormal DRE
(See Page 10 for Position Statement on Early Detection of Prostate Cancer)
• Symptoms which led to PSA/DRE
• Identified by Primary Care Physician
Patient should be given patient education materials ('Reef Knot' package or equivalent) on diagnosis by urologist
• to assist with access to community services and peer support
• patient education materials
• Nova Scotia 'Reef Knot' program- call CCNS for details
Referral to Urologist
Assess current sexual function and discuss potential impact of treatment options (e.g. sexual dysfunction, incontinence) and impact on patients and partners
Prostate biopsy
• Biopsy sample to Pathology Lab
No Invasive Cancer Present
Continue to follow PSA levels (by Urologist or Family Physician) +/- biopsies
Invasive Cancer Present
Staging Investigations
• Serum PSA levels
• Consider bone scan (if PSA >10 ng/mL, or if Gleason Grade ≥ 7, if disease is locally advanced, or if there are symptoms suggestive of metastases)
• CT or MRI pelvic scans, if PSA > 20 ng/mL
• Pelvic lymph node dissection, if PSA > 20 ng/mL, or if PSA > 10mg/L and Gleason Grade > 7
Management by Risk Category
Referral to Cancer Centre if Radiotherapy and/or Chemotherapy under consideration
• See Page 2 for details

Staging Prostate Cancer

TNM- T (Tumour) N (Node) M (Metastasis) Criteria

Clinical Tumour Size (T):

T0 No evidence of a primary tumour
T1 Clinically inapparent tumour, neither palpable nor visible by imaging
T2 Tumour confined within prostate
T3 Tumour extends through prostate capsule
T4 Tumour is fixed or invades adjacent structures

Pathologic Tumour Size (pT):

pT1 *There is no pathologic T1 classification*
pT2 Organ confined
pT3 Extraprostatic extension
pT4 Invasion of bladder, rectum

Clinical Node Involvement (N):

N0 No metastasis to regional lymph nodes
N1 Metastasis in regional lymph node(s)

Pathologic Node Involvement (pN):

pN0 No positive regional lymph nodes
pN1 Metastasis in regional lymph node(s)

Presence of Metastasis (M)

M0 No distant metastasis
M1 Distant metastasis present

Grading Criteria

Prostate adenocarcinomas are graded by the Gleason score: scores in the range 2-10.

- Well differentiated tumours (Gleason 2-6)
- Moderately differentiated tumours (Gleason 7)
- Poorly differentiated tumours (Gleason 8-10)

Grading not generally used for staging at Capital Health

Stage I	T1a	N0	M0	Low Grade
Stage II	T1	N0	M0	Any Grade
	T2	N0	M0	Any Grade
Stage III	T3	N0	M0	Any Grade
Stage IV	T4	N0	M0	Any Grade
	Any T	N1	M0	Any Grade
	Any T	Any N	M1	Any Grade

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Referral Criteria for Prostate Cancer

Referral to Cancer Centre if Radiotherapy and/or Chemotherapy under consideration

Local Urologist

- Refer as per usual practice within local community or health care district

QEII Health Sciences Centre:

- Faxed referrals to the QEII Cancer Care Program (CCP) Referrals Office at 902-473-6079 (tel. 902-473-5140 or 902-473-6098).

Cape Breton Cancer Centre:

- Direct referrals to the Referrals/Booking office at 902-567-7774 (fax. 902-567-7911).

Urgent Referrals:

- For urgent or emergent referrals, in Halifax- page the appropriate specialist on call through the Locating service (902-473-2220); in Cape Breton- page the appropriate specialist on call through the Locating service (902-567-8000)

Referral Information:

- Letter of Referral*
- Laboratory Results*- CBC, PSA (including old results)
- Biopsy Pathology Reports
- Operative Reports (prostatectomy, orchiectomy, other)
- Diagnostic Imaging Reports (TURP, bone scans, chest X-ray, CT scans, other)

* *Specific information which is necessary for proper triage of referrals*

Initial Treatment Options for Prostate Cancer

Low Risk:
T1-T2a
and
Low PSA (<10 ng/mL)
and
Low Gleason Grade (≤6)

- Prostatectomy
- External beam radiotherapy alone
- Brachytherapy (seed implant- not available in NS)
- Expectant Management
- Observation

Intermediate Risk:
T2b-T2c
or
PSA = 10-20 ng/mL
or
Gleason Grade = 7

- Neoadjuvant Androgen Deprivation Therapy (ADT) and radical external beam radiotherapy (RT) (ADT for 2-8 months prior to RT or concurrent witn RT)
- Dose-escalated conformal external beam (3D) radiotherapy
- Prostatectomy
- ADT as primary treatment if contraindication to radiotherapy and prostatectomy
- Expectant Management
- Observation (for patients with significant morbidity or poor life expectancy)

High Risk:
T3-T4
or
Gleason Grade ≥8
or
PSA >20 ng/mL

- Neoadjuvant ADT and external beam radiotherapy (including elective treatment of pelvic lymph nodes) PLUS 2 years adjuvant hormone treatment
- Prostatectomy (for highly selected patients with low volume disease; NOT RECOMMENDED for T3b-T4 patients) Post operative radiotherapy and/or ADT may be required
- ADT as primary treatment in very high risk patients with low chance of cure
- Observation (for patients with significant morbidity or poor life expectancy)

Observation

- Observation consists of medical follow up where it is unlikely that the patient will be treated with radiation therapy or surgery for cure due to a limited life expectancy or severe medical co-morbidities. Treatment at symptomatic progression will likely consist of ADT with additional interventions given with the intent of improving impairments in prostate cancer-specific health-related quality of life.

Expectant Management

- Expectant management involves actively monitoring the course of disease with the expectation to intervene if the cancer progresses or if symptoms become imminent.
- Patients with clinically localized cancers that are candidates for definitive treatment and choose expectant management should have regular follow up.
  - DRE and PSA every 6 months
  - Needle biopsy of the prostate may be repeated within 6 months of diagnosis if initial biopsy was < 10 cores or assessment discordant (eg, palpable tumour contralateral to side of positive biopsy).
  - Needle biopsy should be performed within 18 months if > 10 cores obtained initially, then periodically
- A repeat biopsy may be indicated for any sign of disease progression by exam or markers.

Follow-Up After Curative Therapy

- The goal of follow up is to detect recurrence and to monitor for side effects from the treatment.
- Followup visits should include reassessment and management of supportive care issues, including psychosocial, sexual and/or incontinence problems.
- Follow up schedule will depend on a number of factors:
  - the initial clinical or pathological stage of the disease
  - acute or chronic toxicities
  - post therapy PSA levels, or rising PSA levels

After Curative Radiotherapy

Frequency	Provider	Tests	Year 1-5
every	6-24 months	RO	Clinical assessment, DRE
1-5	every 3-4 months	RO	PSA *
>5	every 1-3 years	RO	Clinical assessment, DRE
>5	every 3-6 months	RO	PSA

* Serum testosterone may be monitored in patients receiving ADT

After Curative Radical Prostatectomy

Year	Frequency	Provider	Tests
1-3	every 3-12 months	U	PSA, Clinical assessment
3- Ongoing	every 6-12 months	U	PSA, Clinical assessment

RO: radiation oncologist U: urologist
DRE: digital rectal examination PSA: prostate specific antigen

ADT (Androgen Deprivation Therapy - Hormonal Regimens)

The choice of initial orchiectomy or androgen deprivation (hormonal) agent(s) for any individual patient will depend on many factors.

- Combined Androgen Blockade (CAB- LHRH agonist plus non-steroidal antiandrogen agent) is not routinely indicated.
- Monotherapy with nonsteroidal antiandrogens is not routinely indicated.
- After initial failure of ADT, secondary hormonal manipulation should be tried (eg. addition of a non-steroidal antiandrogen or discontinuation of non-steroidal antiandrogen if already on).
- Other hormonal manipulations, such as ketoconazole or estrogens may be tried. Some phase II trials show a decline in PSA. There are no randomized data to support any survival advantage.

OPTIONS:

1. Orchiectomy

The testicles are surgically removed. The procedure is done as an outpatient, usually done under local anesthetic. Surgical castration (orchiectomy) is permanent.

2. LHRH Agonists

Goserilin (Zoladex®) 3.6 mg SC Depot q28d OR 10.8 mg SC Depot q84d
Leuprolide (Lupron®-IM, Eligard®-SC) 7.5 mg IM/SC Depot q28d
OR 22.5 mg IM/SC Depot q84d (3mo) OR 30 mg SC Depot q112d (4 mo)
OR 45 mg SC Depot q168d (6mo)
Buserilin (Suprefact®) 6.3 mg SC Depot q56d OR 9.45 mg IM Depot q120d
Note: Due to an initial rise in testosterone levels, patients should be given a non-steroidal antiandrogen (see below) for 2-4 weeks at the same time as their first LHRH agonist dose

3. Non-steroidal Antiandrogen Agents

Flutamide (Euflex®) 250 mg PO TID
Bicalutamide (Casodex®) 50 mg PO daily, up to 150 mg PO daily to TID
Nilutamide (Anandron®) 50 mg PO BID or TID

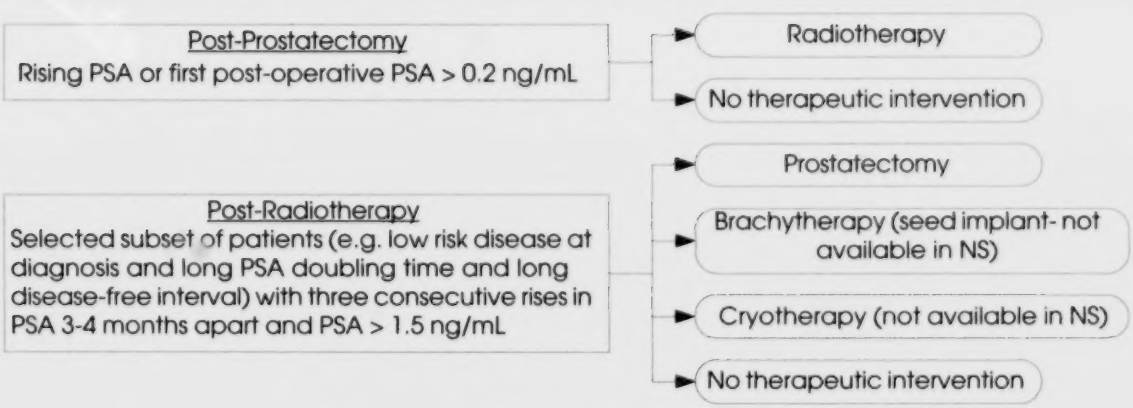
4. Other Hormonal Treatments

Cyproterone (Androcur®) 50-100 mg PO BID or TID
Megestrol (Megace®) 80-160 mg PO daily
Ketoconazole (Nizoral®) 400 mg PO TID (+/- Hydrocortisone 20 mg qAM & 10 mg qPM)
Estrogens- e.g. Diethylstilbestrol 1 mg PO Daily

Post-Prostatectomy Management

Post-operative PSA Undetectable or PSA < 0.2 ng/mL
Assess effect of treatment(s) on patient function (especially incontinence & sexual dysfunction) and psychosocial distress. Manage symptom(s) and distress as appropriate
pT2, pT0 NX,N0 M0 negative margin
No therapeutic interventions, standard follow-up management
pT2 (positive margin), pT3a NX,N0 M0
No therapeutic interventions, standard follow-up management
Radiation Therapy (+/- ADT)
pT3b NX,N0 M0
ADT alone
Radiation Therapy (+/- ADT)
No therapeutic interventions, standard follow-up management
pT4 NX,N0 M0
Radiation Therapy (+/- ADT)
ADT alone
No therapeutic interventions
pTX N+ M0
ADT alone
No therapeutic interventions, standard follow-up management
Post-operative PSA Detectable PSA ≥ 0.2 ng/mL
See Salvage Therapy

Salvage Therapy


Post-Prostatectomy
Rising PSA or first post-operative PSA > 0.2 ng/mL
Radiotherapy
No therapeutic intervention
Post-Radiotherapy
Selected subset of patients (e.g. low risk disease at diagnosis and long PSA doubling time and long disease-free interval) with three consecutive rises in PSA 3-4 months apart and PSA > 1.5 ng/mL
Prostatectomy
Brachytherapy (seed implant- not available in NS)
Cryotherapy (not available in NS)
No therapeutic intervention

Metastatic and Incurable Prostate Cancer

Metastatic cancer or clinically detectable lymph node disease
- Immediate ADT
- Delayed ADT

High-risk disease (without proven metastases)
- Unlikely to be cured and/or
- Significant co-morbid disease

→ Immediate or delayed ADT

Consider referral to Palliative Care service (see page 9) and/or provincial home care service

Hormone Refractory Prostate Cancer

Prostate cancer managed with ADT
- Rising PSA and/or
- Worsening radiographic disease and/or
- Worsening symptoms

→ Castrate Testosterone Level

Yes → Secondary Hormonal Treatment

No → Implement effective ADT

Secondary Hormonal Treatment:
- Addition of anti-androgen agent to LHRH agonist or orchiectomy
- Discontinuation of anti-androgen (if already on one)
- Other Hormonal Treatment:
  - Cyproterone
  - Megestrol
  - Ketoconazole
  - Estrogen

→ Persistent pain or other symptoms

- Optimize analgesic therapy for pain management (see *CCNS* Guidelines for Management of Cancer-Related Pain)
- Urological intervention (e.g. TURP)
- Radiotherapy (localized or hemi-body)
- Low dose steroids (e.g. prednisone 5-10 mg/day or dexamethasone 1-2 mg/day)
- Systemic radionuclides (e.g. Strontium 89) See Comprehensive Version Appendix X
- Chemotherapy (docetaxel plus prednisone or mitoxantrone plus prednisone)
- Bisphosphonate therapy (e.g. zoledronic acid 4 mg IV)

Management of Sexual Dysfunction

Pre-treatment assessment for normal sexual function

↓

Initiate post-operative/post-treatment discussions (6-12 weeks after treatment):

- Consider institution of oral agents (sildenafil (Viagara®), tadalafil (Cialis®), vardenafil (Levitra®)) to conserve penile health
  - Urologist/radiation oncologist

↓

At 3-12 months post-treatment:

- Assess efficacy of oral agents and need for sexual function
- If ineffective, consider penile injection therapy
  - Erectile Dysfunction clinic or urologist/radiation oncologist
- Consider couple counselling as appropriate

↓

Reassess at 12 months:

- Sexual function, distress issues

Management of Incontinence

Pre-treatment visit:

- Assessment of bladder function
- Instruction on Kegel exercises
- Training on incontinence products
- Discussion with patient about incontinence

↓

2-3 weeks post-operation (at time of catheter removal):

- Discussion with patient about incontinence
- Patient demonstration of Kegel exercises

↓

Three months post-treatment:

- Discussion with patient about any incontinence
- Referral for Urodynamic studies, if necessary

↓

One year post-treatment:

- Reassess level of continence, consider incontinence device if necessary

See Management of Psychosocial Issues (Full Version Part 8.12)

Management of Psychosocial Issues

Screening for Psychosocial Distress at diagnosis, and other significant transition points

Screening and intervention should include both the patient and his partner

Risk factors for psychosocial distress (e.g. depression, anxiety, adjustment disorders) in prostate cancer

Risk factors for distress:
- age < 60
- mental health history
- social isolation
- receiving ADT
- high burden of illness
- advanced stage of cancer
- unresolved urinary incontinence
- high sexual dissatisfaction
- multiple life stressors

Low Risk

High Risk

Periodic screening at diagnosis, six months after treatment completion, disease recurrence, progression to advanced disease

Routine screening at each visit through disease continuum

Referral as appropriate for identified psychosocial distress problem(s)

Management of Pain and Other Symptoms

Referral of a cancer patient who needs help with pain or symptom management, or for palliative care

To The Attending Oncology Team:
- See Full Version Page 23

To The Cancer Patient Navigator:
- 1-866-524-1234 from anywhere in Nova Scotia

To The District Palliative Care/Supportive Care Service:

South Shore Health:
- 902-634-7369 or 902-354-3436

South West Health:
- 902-742-3542 Ext. 414.

Annapolis Valley Health:
- 902-678-7381 Ext. 2270

Colchester East Hants Health Authority:
- 902-893-5554 Ext. 2306

Cumberland Health Authority:
- 902-667-5400 Ext. 6373

Pictou County Health:
- 902-752-7600 Ext. 4190

Guysborough Antigonish Strait Health Authority:
- 902-867-4296 or 902-867-4436

Cape Breton District Health Authority:
- 902-567-7846

Capital Health Cancer Care Program:
- 902-473-3119

Position Statement on Early Detection of Prostate Cancer

Background

Prostate cancer is the most commonly diagnosed cancer and the second leading cause of cancer deaths in Canadian men. Nova Scotia has the third highest rate of deaths from prostate cancer in Canada.

CCNS Position on Early Identification of Prostate Cancer

Cancer Care Nova Scotia does not at this time support the implementation of a comprehensive population-based prostate cancer screening program for Nova Scotia. While we know that the PSA test may be used to detect early stage prostate cancer, there is insufficient evidence to suggest at this time that a decline in mortality rates from prostate cancer can be directly attributed to screening. As new evidence emerges, this statement will be re-evaluated.

Cancer Care Nova Scotia believes that early identification of prostate cancer requires a partnership between Nova Scotian men and their physicians.

- Men need to be aware of prostate cancer, and what it may mean for them.
- Men who have concerns about prostate cancer should discuss them with their physician.
- Physicians should discuss the potential benefits of early detection of prostate cancer with men over 50 who do not exhibit urological symptoms and those who are considered to be at greater risk for prostate cancer.

The risk of prostate cancer increases with age, especially after the age of 50. Men who have a family history of prostate cancer are more likely to develop prostate cancer. American evidence suggests that men of African heritage are at higher risk of prostate cancer. Physicians are encouraged to discuss the risks and benefits of prostate screening with men in a higher risk category beginning at the age of 40.

Early detection of prostate cancer involves the use of both the Digital Rectal Exam (DRE) and serum PSA determination. The PSA blood test may be used to detect prostate cancers at an early stage. This test is available to Nova Scotian men through their family physicians and following a discussion of the risks and benefits of prostate cancer screening. Men who have difficulty accessing this test through their physician should request a referral to another physician. It is important to recognize that PSA is accepted to be useful in the evaluation of symptomatic prostate disorders.

Guidelines for Health Professionals

The Genito-Urinary (GU) Cancer Site Team recommends that:

- Health professionals be aware of prostate cancer as the most common cancer in men.
- Health professionals recognize the increasing incidence of clinically significant prostate cancer reflecting the increased life expectancy of the current male population.
- Health professionals be aware of the natural history of prostate cancer. It is not advised to screen patients with significant co-morbidities or a limited life expectancy.
- Early detection of prostate cancer involves both the DRE and serum PSA determination.
- Age adjusted PSA reference values be the standard when PSAs are ordered.
- Appropriate counselling (including the risks and benefits of prostate cancer screening) be provided to men prior to initiating screening and that informed consent should be documented.
- Men who choose to be screened should be screened on an annual basis. The need for screening be re-evaluated as necessary based on the man's health status.
- Student physicians continue to be trained in the technique of proper male genitourinary examination including DRE, and learning opportunities for practicing physicians be provided.
- Men who present with urological symptoms or have suspicious findings on physical examination require appropriate diagnostic investigations, including age-adjusted PSA and DRE regardless of age.

This statement was developed by the Genito-Urinary Cancer Site Team of Cancer Care Nova Scotia, with input from provincial stakeholders including health professionals and prostate cancer consumers.

Release date: January, 2002.

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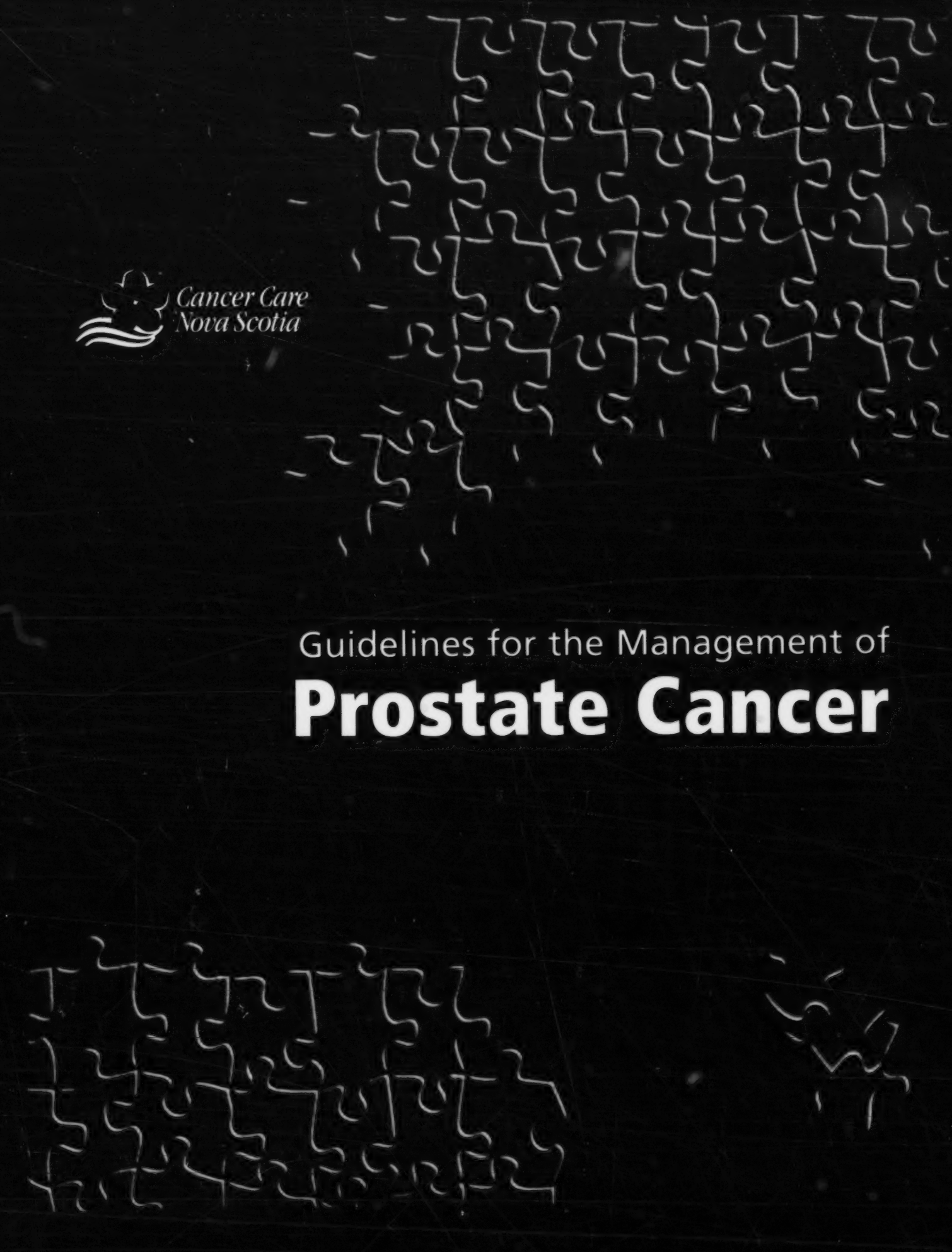
www.cancercare.ns.ca



Guidelines for the Management of

Prostate Cancer

Cancer Care
Nova Scotia

Guidelines for the Management of

Prostate Cancer

Full Version

Guidelines For The Management of Prostate Cancer

Objective:
This guideline reviews the overall management (from initial presentation and diagnosis through referral, treatment and follow up) of prostate cancer in Nova Scotia. This guideline was written for an audience of *general practitioners and medical students*, not necessarily prostate cancer specialists. As such, it is a synthesis of knowledge and evidence, and reflects the practice policies of the Genitourinary Cancer Site Team in Nova Scotia (see Appendix I). A simplified discussion with flowcharts (practice pathways) will summarize the written contents.

Patients, family members and other non-health professionals are encouraged to review materials written specifically for them. The Canadian Cancer Society Information Service (1-888-939-3333 or www.cancer.ca) is one source for this type of information.

Preamble Note:
Practice guidelines are intended to assist health care professionals with decisions throughout the spectrum of the cancer experience. This guideline is intended to assist health care professionals to care for patients with prostate cancer.

Guidelines should never replace specific decisions for individual patients, and do not substitute for the shared decisions between any patient and doctor (or other health professional) which are unique to each circumstance. Guidelines do provide evidence-based background information, consensus-based recommendations for similar problems, and a context for each individual decision.

This guideline will be reviewed in three years from publication date or earlier if important new evidence becomes available. Current versions of this guideline will be available on the *Cancer Care Nova Scotia* website (www.cancercare.ns.ca).

These guidelines are designed for health care professionals, working in a variety of settings. For front-line health care givers, the "Quick Reference Version" of the guidelines will be a useful reminder of assessment and treatment. This version will be useful for those who prefer to read more about the recommendations. The full evidence-based discussions of these guidelines are located in the Appendices, available on request or at the *Cancer Care Nova Scotia* website. Development of these guidelines is described in Appendix II.

Comment on Clinical Research:
An important component of treatment decision-making for any patient is the potential for enrollment in relevant clinical research. The Genitourinary Cancer Site Team is committed to advancing patient care, through participation in clinical trials and other clinical research projects. At any point in time, there may be a clinical trial or other clinical research opportunity related to any component of this guideline. As specific trials or clinical research projects become available, eligible patients may be offered the opportunity to enroll in the relevant trial or research project. Every effort will be made to accommodate patients for clinical research participation, but there will be eligibility restrictions for each trial. Patients are encouraged to discuss clinical trials opportunities with their cancer specialist. Other researchers may also contact patients to offer participation in relevant trials. Current clinical trials are listed on the *Cancer Care Nova Scotia* website (www.cancercare.ns.ca).

Acknowledgements:
This guideline was written by a collaborative effort of the Genitourinary Cancer Site Team, and was sponsored by *Cancer Care Nova Scotia*. Portions of this practice guideline have been adapted from guidelines prepared by the British Columbia Cancer Agency and by the

Cancer Care Nova Scotia

National Comprehensive Cancer Network. The guidelines also incorporate knowledge of current evidence by the cancer experts in Nova Scotia.

For further information on this, or any other Practice Guideline, please contact the CST Co-Chairs, or members of the Guidelines Resource Team, *Cancer Care Nova Scotia* (Tel. 1-866-599-2267 or by e-mail info@ccns.nshealth.ca)

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Guideline Approvals:

- Genitourinary Cancer Site Team-
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  - Revision with Community Reviewer Input- *23 January 2006*
- Cancer Care Nova Scotia, Commissioner- *15 February 2006*

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Part 1. Introduction

1.1 Epidemiology

In males, prostate cancer is the most common non-cutaneous cancer diagnosed, and the second most common cause of cancer death. Age specific incidence[1] of prostate cancer increased steeply in men over the age of 60 (Figure 1). Age-standardized incidence[1] increased dramatically in the early 1990's, most likely due to improved detection through the use of the Prostate Specific Antigen (PSA) test (Figure 2). Age-standardized mortality[1], however, has not changed significantly over the same time period of reporting (Figure 3).

Survival rates of men with prostate cancer[1] are substantially better than the other two leading cancers in men, lung cancer and colorectal cancer (Figure 4). The overall five year survival rate for prostate cancer patients in Nova Scotia was 93%. Survival for prostate cancer patients[1] was dependant on the stage of the cancer at diagnosis, ranging from 99% five-year survival for local malignancies to 27% for patients with distant metastases (Figure 5). Fortunately, over half of the patients (53%) were diagnosed with local disease.

Figure 1. Age-specific incidence rate for common tumour sites, males, Nova Scotia 1995-1999

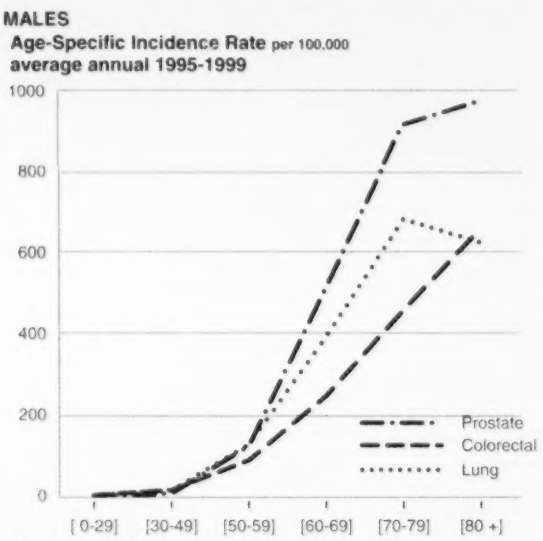


Figure 2. Trends in age-standardized incidence rates for common tumour sites, males, Nova Scotia 1971-1999

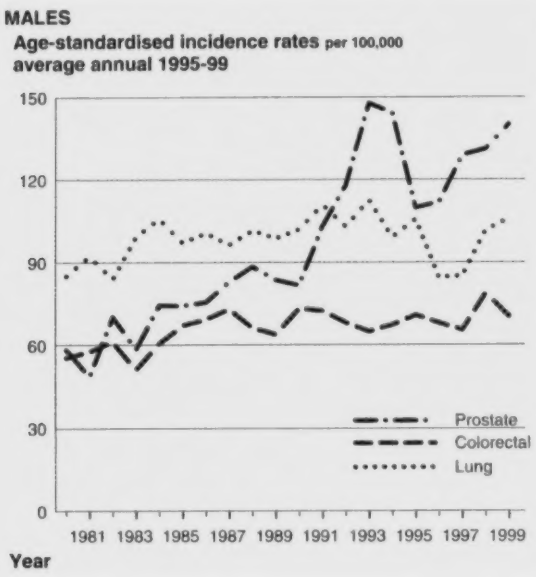


Figure 3. Trends in age-standardized mortality rates for common tumour sites, males, Nova Scotia 1971-1999

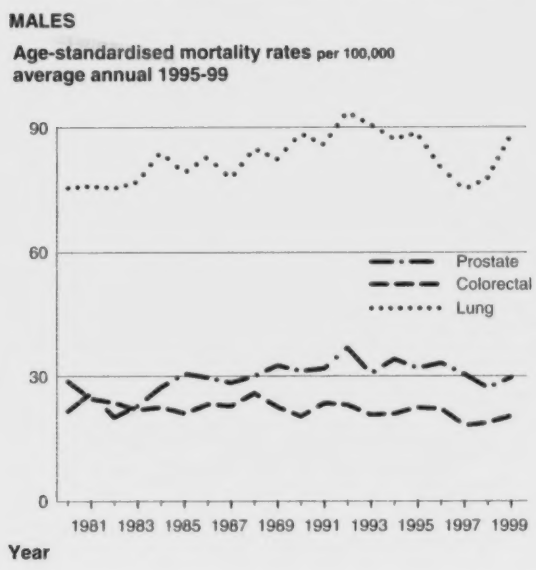


Figure 4. Five-year relative survival for common tumour sites, males, Nova Scotia 1992-1996

The total number of cases (N) retained for analysis appears in parenthesis and a 95% confidence interval (⊢—⊣) is presented for each estimate.

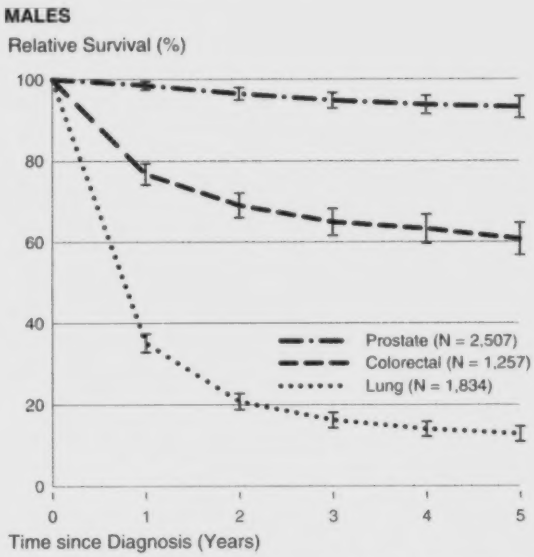
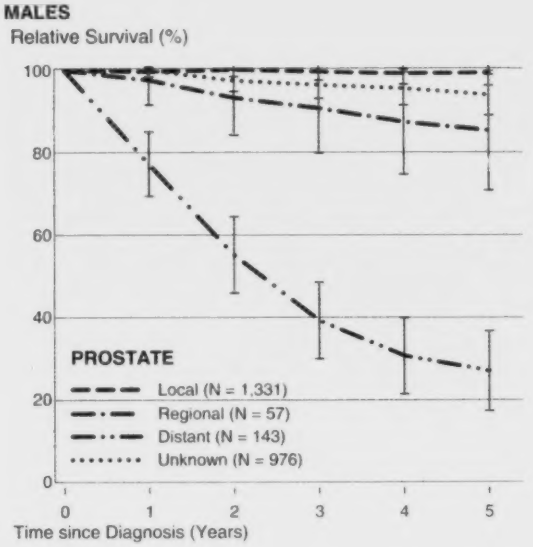


Figure 5. Prostate cancer survival by extent of disease, males, Nova Scotia 1992-1996

The total number of cases (N) retained for analysis appears in parenthesis and a 95% confidence interval (⊢—⊣) is presented for each estimate.



1.2 Risk Factors

The lifetime risk of developing prostate cancer is approximately 10% and the risk of cancer related mortality is 3%. Risk of prostate cancer is higher in males with a first degree relative with prostate cancer.

1.3. Presentation

Patients may present with an elevated PSA without symptoms, with an asymptomatic prostate abnormality on digital rectal examination (DRE), or with lower urinary tract symptoms. Patients with metastatic disease or locally advanced disease may present with other symptoms referable to the sites of disease involvement (i.e. bone pain, visceral or lymphatic obstruction).

1.4 Screening[2,3,4]

See appendix II (*CCNS* – Prostate Screening Position Statement)

1.4.1 Prostate Specific Antigen (PSA) Reference Ranges:

Normal values for PSA increase with age, as follows[5]:

40-49 yrs	less than 2.5 ng/mL
50-59 yrs	less than 3.5 ng/mL
60-69 yrs	less than 4.5 ng/mL
70-79 yrs	less than 6.5 ng/mL

1.4.2 Sensitivity And Specificity Of PSA Testing And Role Of Free PSA In Determining Risk Of Cancer:

PSA testing sensitivity is approximately 67.5% to 80% (using 4.0 ng/mL as the upper limit of normal). If only PSA testing is used for screening, 20% to 30% of tumours will be missed. To improve sensitivity, a number of methods have been suggested, including: i) digital rectal exam (DRE) for early detection screening; ii) age-adjustment of PSA, using lower limits for younger men (see Section 1.4.1.1); and iii) PSA velocity (rate of PSA change) as a prompt for biopsy. A PSA velocity of 0.75 ng/mL per year may indicate the presence of prostate cancer. These three methods increase the sensitivity of early detection, but also increase the number of prostate biopsies performed.

Improving the specificity of early detection should reduce the number of unnecessary biopsies. To improve specificity, other methods have been suggested, including: i) using higher PSA cut-off levels for men over 60 years old; ii) using percent-free-PSA levels; and iii) using PSA density. Prostate cancer patients have lower fractions of free PSA relative to total PSA measured. Men with elevated PSA levels, but with a ratio of free/total PSA >20% to 25% have significantly lower risk of prostate cancer found on biopsy.

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Part 2. Histology & Pathology

2.1 Histology

The vast majority of neoplasms of the prostate are adenocarcinomas. Occasionally, other histologies (sarcoma, transitional cell carcinoma, small cell carcinoma) may be seen. Prostate adenocarcinomas are typically graded by the Gleason score[1,2]: scores graded in the range 2-10. Tumours may also be divided as well differentiated (typically Gleason 2-6), moderately differentiated (Gleason 7), and poorly differentiated (Gleason 8-10). Tumour grade is a strong prognostic factor in both treated (surgery or radiation) patients as well as patients where observation is elected. To note, a Gleason score should not be assigned to biopsy specimen showing prostate cancer after the patient has been placed on androgen deprivation or finasteride (Propecia®, Proscar®).

2.2 Pathology

2.2.1 Pathologic Assessment of Prostate Biopsy:

The pathology report for needle biopsy specimens[3,4] should include the following information:

- A comment concerning the adequacy of the specimen
- The presence or absence of malignancy
- The histologic type
- The histologic grade (Gleason Score)
- The presence or absence of perineural/lymphatic/vascular invasion
- Extension beyond the prostatic capsule into fat, if present
- Number of cores involved and percentage of surface area of cores submitted
- The presence of high grade Prostatic Intraepithelial Neoplasia (PIN), Atypical Small Acinar Proliferation (ASAP)

2.2.2 Pathological Assessment of TURP Specimens:

Reports on transurethrally resected specimens should include the information required when reporting needle biopsy specimens, and in addition should include the percentage of chips showing tumour.

2.2.3 Pathological Assessment of Radical Prostatectomy Specimen:

Radical prostatectomy specimen resection margins should be marked with ink and these should be sampled generously. Obvious tumours should be sampled and random sections of apparently normal prostatic tissue should be taken. Pathology reports should include the following information:

- AP, lateral, and apex to base dimensions of the prostate gland in centimeters
- The presence or absence of tumour
- The extent and location of tumour
- The histologic type
- Gleason patterns and score
- The presence of high grade PIN (prostatic intra-epithelial neoplasia)
- The presence or absence of vascular/lymphatic/perineural invasion
- The presence or absence of extraprostatic extension
- The status of the surgical margins (involved versus clear)
- Seminal vesicle invasion
- The presence or absence of nodal involvement, number of nodes examined, presence of extranodal extensions (if sampled)

Table 2.1 Gleason Grading System For Prostatic Adenocarcinoma: Histologic Patterns[2]

Pattern	Peripheral Borders	Stromal Invasion	Appearance of Glands	Size of Glands	Architecture of Glands	Cytoplasm
1	Circumscribed pushing expansile	Minimal	Simple, round, monotonously replicated	Medium, regular	Closely packed rounded masses	Similar to benign epithelium
2	Less circumscribed; early infiltration	Mild, with definite separation of glands by stroma	Simple, round, some variability in shape	Medium, less regular	Loosely packed rounded masses	Similar to benign epithelium
3A	Infiltration	Marked	Angular with variation in shape	Medium to large	Variable packed irregular masses	More basophilic than patterns 1 & 2
3B	Infiltration	Marked	Angular with variation in shape	Small	Variable packed irregular masses	More basophilic than patterns 1 & 2
3C	Smooth, rounded	Marked	Papillary and cribriform	Irregular	Round to elongate masses	More basophilic than patterns 1 & 2
4A	Ragged infiltration	Marked	Microacinar, papillary and cribriform	Irregular	Fused with chains and cords	Dark
4B	Ragged infiltration	Marked	Microacinar, papillary and cribriform	Irregular	Fused with chains and cords	Clear (hypernephroid)
5A	Smooth, rounded	Marked	Comedocarcinoma	Irregular	Round to elongate masses	Variable
5B	Ragged infiltration	Marked	Difficult to identify gland lumens	Irregular	Fused sheets and masses	Variable

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Part 3. Diagnosis and Staging

3.1 Diagnosis- Prostate Biopsy:
An elevated PSA or abnormal DRE may indicate increased risk of prostate cancer, but they cannot determine a diagnosis of prostate cancer. The only method to confirm the presence of prostate cancer is a prostate biopsy. Usually, a prostate biopsy is performed transrectally with ultrasound guidance. Transrectal ultrasound (TRUS) has poor ability to diagnose prostate cancer[1], so a normal TRUS with abnormal DRE or elevated PSA should not be used as a criterion to avoid prostate biopsy. Prostate cancer is rarely diagnosed at the time of TURP.

3.1.1 Minimum Workup At The Time Of Prostatic Biopsy:

- Full history and physical examination, PSA blood test
- Bilateral biopsy of prostate with at least eight cores sampled. Additional samples may be taken from suspicious nodules or ultrasound abnormality, where appropriate

3.1.2 Indications For Re-Biopsy When No Invasive Cancer Present:

- Focus of ASAP or PIN (see 2.2.1) in a man eligible for curative therapy
- Progressively rising PSA
- Suspicious nodule

3.2 Staging Investigations

- Serum PSA will guide selection of staging studies for newly diagnosed prostate cancer
- Laboratory investigations: hemoglobin, liver function tests, creatinine, testosterone, alkaline phosphatase
- Consider bone scan, if PSA >10 ng/mL, or if Gleason Grade $\geq$ 7, if disease is locally advanced, or if there are symptoms suggestive of metastases[2,3,6,7] (such as weight loss, bone pain)
- CT or MRI[4,5] pelvis scans may be considered if a patient has an increased likelihood of lymph node metastases (>20%), a Gleason score $\geq$8, PSA > 20 ng/mL, T3 or T4 lesion[4-7].
- A pelvic lymph node dissection[8,9] may be performed in very selected cases

Table 3.2.1 T (Tumour) Definitions[10]	
	Clinical:
T X	Primary tumour cannot be assessed
T 0	No evidence of a primary tumour
T1	Clinically inapparent tumour, neither palpable nor visible by imaging T1a Tumour incidental finding in 5% or less of tissue resected T1b Tumour incidental finding in more than 5% of tissue resected T1c Tumour identified by needle biopsy (e.g. because of elevated PSA)
T 2	Tumour confined within prostate (Note: tumour found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging is classified as T1c) T2a Tumour involves one-half of one lobe or less T2b Tumour involves more than one-half of one lobe, but not both lobes T2c Tumour involves both lobes
T 3	Tumour extends through prostate capsule (Note: invasion into the prostatic apex or into, but not beyond, the prostatic casule is classified as T2) T3a Extracapsular extension (unilateral or bilateral) T3b Tumour invades seminal vesicle(s)
T 4	Tumour is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles and/or pelvic wall
	Pathologic (pT):
pT1	*There is no pathologic T1 classification*
pT2	Organ confined pT2a Unilateral, involving one-half of one lobe or less pT2b Unilateral, involving more than one-half of one lobe, but not both lobes pT2c Bilateral disease
pT3	Extraprostatic extension pT3a Extraprostatic extension (positive surgical margin indicated by an R1 descriptor- residual microscopic disease) pT3b Seminal vesicle invasion
pT4	Invasion of bladder, rectum

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Table 3.2.2 N (Node) Definitions[10]	
	Clinical:
NX	Regional lymph nodes were not assessed
N0	No metastasis to regional lymph nodes
N1	Metastasis in regional lymph node(s)
	Pathologic (pT):
pNX	Regional lymph nodes not sampled
pN0	No positive regional lymph nodes
pN1	Metastasis in regional lymph node(s)

Table 3.2.3 M (Metastasis) Definitions[10]	
MX	Distant metastasis cannot be assessed (not evaluated by any modality)
M0	No distant metastasis
M1	Distant metastasis present M1a Non-regional lymph node(s) M1b Bone(s) M1c Other site(s) with or without bone disease

Stage Groupings: TNM Subsets*[10]				
Stage I	T1a	N0	M0	G1
Stage II	T1a	N0	M0	G2, 3-4
	T1b	N0	M0	Any G
	T1c	N0	M0	Any G
	T1	N0	M0	Any G
	T2	N0	M0	Any G
Stage III	T3	N0	M0	Any G
Stage IV	T4	N0	M0	Any G
	Any T	N1	M0	Any G
	Any T	Any N	M1	Any G

* Grading not generally used for staging at Capital District Health Authority

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Part 4. Referral Information for the New Patient Visit

A letter of referral and a pathology report documenting the cancer diagnosis are the usual minimal requirements for a referral of adult patients to a tertiary cancer center. A referral need not be delayed due to incomplete results from tests (either due to test scheduling delays or waiting time for test results).

Local Urologist

- Refer as per usual practice within local community or health care district

Referral to the QEII Health Sciences Centre

Referrals to the Capital Health/QEII Cancer Care Program (CCP) may be faxed to the Referrals Office at 902-473-6079 (tel. 902-473-5140 or 902-473-6098). It is preferred that referrals be accompanied by the CCP Referral Form available upon request at the above phone numbers or available for downloading at www.cdha.nshealth.ca/physicianupdate. For urgent or emergent referrals, please page the appropriate specialist on call through the QEII HSC Locating service (902-473-2220) to discuss the referral.

Referral to the Cape Breton Cancer Centre

Referrals to the Cape Breton Cancer Centre may be directed to the referrals/booking office at 902-567-7774 (fax 902-567-7911). For urgent or emergent referrals, please page the appropriate specialist on call through the Cape Breton Regional Hospital Locating service (902-567-8000) to discuss the referral.

Referral Information

Letter of Referral*

A legible referral or consultation letter highlighting presenting signs, symptoms and pertinent findings

Laboratory Results*

a. Serum PSA (prostate specific antigen) levels- including old results*
b. CBC (complete blood counts)

Biopsy Reports*

a. Prostate biopsy reports
b. TURP biopsy reports

Operative Reports (relevant to the cancer)*

a. Prostatectomy
b. Orchiectomy
c. Other procedures

Diagnostic Imaging Reports*

a. Transrectal Ultrasound of prostate-reports*
b. Bone scans (with films) *
c. Any relevant chest radiographs (with films)
d. Any relevant CT scans
e. Any other relevant diagnostic imaging

Other Information

a. Any relevant consultation reports
b. Renal function test results (if done)
c. Relevant bloodwork: BUN, creatinine, calcium (if done)
d. Detailed information on any previous chemotherapy or radiotherapy of current malignancy
e. Any information on previous malignancies
f. Information on co-existing medical conditions and allergies

* Specific information which is necessary for proper triage of referrals

Please note: If the referring physician would like to discuss a case with a specialist, feel free to call the appropriate specialist (Radiation Oncology, Medical Oncology, or Urology, by calling 902-473-2222- ask for the specialist on call or a specific physician at this number). If any tests or reports are pending, the date of the procedure, and the location of the procedure should be noted, so that the reports may be obtained when available. Send in the referral while awaiting these results, to facilitate a timely appointment for your patient.

Part 5. Treatment

Note: For optimal patient care, psychosocial management is integrated with medical/surgical management of the disease and symptoms.

5.1 Curative Treatment Options By Risk Category:

Pretreatment PSA[1-8], grade[9-13] and clinical stage are prognostic factors for outcome following surgery[14-16], radiotherapy[17-21], expectant management[22-25] (See Appendix III for principles of expectant management) or observation[26,27] (See Appendix IV for principles of observation) for non-metastatic disease. Various prognostic schemes combining different categories of these factors have been proposed[28-31] and, in general, these schemes stratify patients into low, intermediate and high risk categories. Low risk patients have a high chance of disease control with single modality therapy (or expectant management in selected patients); high risk patients have a high chance of systemic failure with localized treatment modalities and should be considered for adjuvant therapy. Treatment of intermediate risk patients is controversial.

5.2 Definition Of Risk Categories With Treatment Options[32]:

5.2.1 Low Risk

T1-T2a
and
Low PSA (< 10ng/mL)
and
Low Gleason Grade (≤ 6):

Treatment Options:

Patients may choose one of these options in discussion with their doctor[13,33]

- Radical prostatectomy[14,16,34-38] (see Appendix V)
- External beam radiotherapy alone[38-44] (see Appendix VI - Comprehensive Version)
- Brachytherapy[45-47] (seed implant- see Appendix VI- Comprehensive Version)
  - not available in Nova Scotia
- Expectant Management[22,48-51]
- Observation[13,52-54]

5.2.2 Intermediate Risk:

T2b-T2c
or
PSA = 10-19 ng/mL
or
Gleason Grade = 7:

Treatment Options:

Patients may choose one of these options in discussion with their doctor[13,33]

- Radical prostatectomy[14,16,25,35-37] with or without pelvic lymph node dissection (PLND)
- Neoadjuvant Androgen deprivation therapy (ADT- also known as hormonal therapy) (see Appendix VII- Comprehensive Version) and radical external beam radiotherapy[55]
  - ADT given for 2-8 months prior to radiotherapy[56]
  - ADT concurrent with radiotherapy may be given[55]
- Dose-escalated conformal external beam radiotherapy (3D)[25,57]
- ADT may be used as primary treatment if contraindication to radiotherapy and radical prostatectomy.
- Expectant Management[53]
- Observation[13,34,53,58]

5.2.3 High Risk:

T3-T4
or
Gleason Grade ≥ 8
or
PSA > 20ng/mL

Treatment Options:

Patients may choose one of these options in discussion with their doctor[59]

- Neoadjuvant ADT[25,55,56,60-62] and external beam radiotherapy (including elective treatment of pelvic

lymph nodes[63,64]) (see Section 5.2.2) with or without 2-3 years of adjuvant ADT[55,56,65-69]

- Radical prostatectomy[70-73] – for highly selected patients with low volume disease; Not recommended for T3b-T4 patients
  - Post operative radiotherapy and/or ADT may be required
- ADT may be used as primary treatment in very high risk patients with low chance of cure[74-76]
- Observation[77]

5.3 Post-Prostatectomy Management

Post-operative PSA Undetectable or PSA < 0.2mg/mL

pT2, pT0 NX,N0 M0 negative margin

- Observation, standard follow-up management[25]

pT2 (positive margin), pT3a NX,N0 M0

Options:

- Radiation Therapy[4,10,78-82] (+/- ADT)
- Observation, standard follow-up management

pT3b NX,N0 M0

Options:

- Radiation Therapy[4,10,78-82] (+/- ADT)
- ADT alone
- Observation, standard follow-up management[25]

pT4 NX,N0 M0

Options:

- Radiation Therapy (+/-ADT)
- ADT alone

pTX N+ M0

Options:

- ADT[25,83]
- Observation, standard follow-up management

Post-operative PSA Detectable

PSA ≥ 0.2 ng/mL – See Salvage Therapy Section 5.4

5.4 Salvage therapy

5.4.1 Salvage Radiotherapy Post-Radical Prostatectomy[25,79,81,84,85]

Should be considered in the setting of rising PSA (on at least two subsequent measurements) after radical prostatectomy (minimum PSA > 0.2 ng/dL) or first post-operative PSA > 0.2 ng/dL in patients who are more likely to have disease isolated to the prostatic bed.

Biochemical relapse-free survival (but not overall survival) is superior if radiotherapy initiated when PSA < 1 ng/dL, and PSA doubling time > 10 months, and PSA recurrence post-prostatectomy > 18 months

5.4.2 Salvage Therapy Post-Radiotherapy[25]

In a highly selected subset of patients (e.g. low risk disease at diagnosis and long PSA doubling time and long disease-free interval) with three consecutive rises in PSA 3-4 months apart[86] ***and*** PSA ≥ 1.5 ng/mL, options may include:

- Prostatectomy
- Brachytherapy/seed implant
  - not available in Nova Scotia
- Cryotherapy
  - not available in Nova Scotia

5.5 Metastatic Cancer of the Prostate

Patients with metastatic or clinically detectable lymph node disease are considered to be incurable and are generally offered immediate ADT[76,87]. This could include:

- LHRH agonist[74,88-93]
- LHRH agonist plus antiandrogen[92-94]
- Orchiectomy[74,95,96]

Other patients who have extremely high-risk disease (without proven distant disease) who are unlikely to be cured and/or those who have significant co-morbid disease may be considered for immediate or delayed ADT alone[55].

5.6 Hormone Refractory Prostate Cancer

Hormone refractory prostate cancer is defined by rising PSA, worsening radiographic disease, or worsening symptoms while on ADT. Castrate testosterone levels should be confirmed (< 1.75 nmol/L) and effective ADT implemented if not the case.

Secondary hormonal manipulations may be indicated. These may include:

- Addition of antiandrogen agent to orchiectomy or LHRH agonist[92-94] (See Appendix VII- Comprehensive Version)
- Discontinuation of antiandrogen if patient has been receiving one[97-100]
- Other less commonly-used manipulations[101] (See Appendix VII- Comprehensive Version)

Symptom control should be optimized, especially analgesic therapy and supportive measures. The palliative care team should be consulted. Other interventions aimed at improving symptom control may include:

- Urological intervention (e.g. TURP)
- Radiotherapy (localized or hemi-body)[102]
- Low dose steroids[103] (i.e., prednisone 5-10 mg/day or dexamethasone 1-2 mg/day)
- Systemic radionuclides[104-106]

(See Appendix X- Comprehensive Version)

- Palliative chemotherapy

(See Appendix VIII- Comprehensive Version)

- Docetaxel plus prednisone[106-107]

(See Appendix IX- Comprehensive Version)

- Mitoxantrone plus prednisone[108]
- Bisphosphonate therapy
  - Data is emerging to indicate zoledronic acid decreases skeletal events (e.g. pathologic fractures, need for radiotherapy, need for surgery, spinal cord compression) and decreases pain in hormone refractory prostate cancer[109].

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Part 6. Follow-up

6.1 Follow-up after Curative Therapy

The goal of follow up after curative therapy is to detect recurrence and to monitor for side effects from the treatment. In addition, followup visits should include reassessment and management of any supportive care issues, including psychosocial, sexual and/or incontinence problems. The follow up schedule after curative radiotherapy or radical prostatectomy will depend on a number of factors[1], including the initial clinical or pathological stage of the disease, acute or chronic toxicities, the post therapy PSA levels, or rising PSA levels. The following schedules are recommended after each of these curative treatments. The physician should review the followup schedule with each patient before completion of initial treatment, so that the patient has an understanding of what to expect.

6.1.1 Follow-up after Curative Radiotherapy

Year	Frequency	Provider	Tests
1-5	every 6-24 months	RO	Clinical assessment, DRE
1-5	every 3-4 months	RO	PSA *
>5	every 1-3 years	RO	Clinical assessment, DRE
>5	every 3-6 months	RO	PSA

* Serum testosterone may be monitored in patients receiving ADT

RO: radiation oncologist, for follow-up of treatment effectiveness and long-term toxicity
DRE: digital rectal examination
PSA: prostate specific antigen

6.1.2 Followup after Curative Radical Prostatectomy

Year	Frequency	Provider	Tests
1-3	every 3-12 months	U	PSA, Clinical assessment
3-Ongoing	every 6-12 months	U	PSA, Clinical assessment

U: urologist
PSA: prostate specific antigen

6.2 Follow-up for patients with Metastatic Disease

The interval, investigations, and providers will be determined by the patient's clinical condition and symptoms.

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Part 7. Supportive Care Issues

7.1 Psychosocial Needs

Prostate cancer patients, like all cancer patients, may have a number of supportive care needs, often including the need for psychosocial support[1,2]. The psychosocial needs will differ from newly diagnosed men, to those living with the cancer, and to those who fail treatment.

Psychosocial support may be needed for help to cope with the cancer experience. For some patients, mental health support may be needed. There is about 25% chance of clinically significant depression, anxiety and adjustment difficulties[3-6]. In addition, one must also pay attention to the impact of the cancer on the patient's partner. Prostate cancer and its treatment may cause or exacerbate erectile dysfunction[7,8], urinary incontinence, a change in mood and sleep patterns. It is the responsibility of the attending health caregivers to provide basic support through the continuum of disease. This should include basic screening for signs of depression[12,13] in the patient. Where available, cancer patient navigators are a valuable resource for patients. There may be peer support groups in local communities to help patients.

Screening for distress (see Section 8.12) should be included in patient visits at diagnosis and other key transition points (e.g. six months after treatment completion, disease recurrence, progression to advanced disease). For high risk patients, distress screening should be included at each visit. Risk factors to consider in selecting the frequency of distress screening include[14]:

- age < 60
- mental health history
- social isolation
- receiving ADT (hormone therapy)
- greater burden of illness
- advanced stage of cancer
- unresolved urinary incontinence
- high sexual dissatisfaction
- multiple life stressors

If possible, partners should be involved in the process of screening for distress.

If there are specific needs beyond the abilities of the front-line caregivers, a referral to the Psychosocial Oncology Team at either of the Cancer Centres, or an appropriate local resource (eg. mental health specialists), may be considered. Specialized psychosocial support may be offered by psychosocial counsellors, psychologists, psychiatrists, social workers, clinical nurse specialists, or other trained professionals.

7.2 Symptom Management

The treatment of prostate cancer is complex and may include surgery, external beam radiotherapy, brachytherapy, ADT, or chemotherapy. These treatments have specific and overlapping side effects, which may affect quality of life. Common side effects include erectile dysfunction, urinary incontinence, loss of libido, hot flashes, and mood swings.

7.2.1 Erectile Dysfunction and Sexual Health

Following prostate cancer treatment, there is a high incidence of erectile dysfunction (ED)[15-19], up to 85% depending on the treatment. Prior to treatment, 30-40% of men report pre-existing ED as a result of other factors[7,8,20]. Therefore, it is important to assess sexual issues prior to treatment, to determine baseline and to identify the degree of concern for the patient and his partner[8-11,21,22]. This assessment can identify many issues beyond baseline ED. It is recommended that the man's partner should be allowed to participate in the pre-treatment assessment[23]. (Query their

current level of sexual activity, how satisfied they are with this and how concerned they are about possible changes.) If necessary, consider initiation of sexual counselling to address aspects of the couple's relationship[24,25].

Following radical prostatectomy or radical radiotherapy, at 6-12 weeks post-treatment, a visit should be planned to discuss possible resumption of sexual activity (including issues such as the return of erections, morning fullness)[26-30]. At this time, consideration may be given to initiate oral therapy with a phosphodiesterase enzyme inhibitor[31-38] (e.g. sildenafil (Viagra®), tadalafil (Cialis®), vardenafil (Levitra®)) to stimulate erectile tissue. It is important to note with the patients that the purpose of these oral agents is to preserve tissue and enhance penile health, not necessarily for sexual relations.

A follow-up visit should be planned for 3-12 months after treatment to discuss the couple's sexual function and satisfaction. If the oral agent is not working, consider prostaglandin injections[39-41] (e.g. alprostadil (Caverject®)) and a referral to erectile dysfunction (ED) clinic (Note: only available in Halifax). Another option could be referral for couples counselling or sex therapy, where available. This should be re-assessed at 12 months, or as necessary.

7.2.2 Urinary Incontinence

Urinary incontinence is another common consequence of prostate cancer treatment[24,25]. This can be very distressing to patients, especially if not addressed early in the treatment. This potential adverse effect should also be discussed before treatment, along with an assessment of pre-treatment bladder function. Patients should be instructed on Kegel exercises and advised on the use of incontinence products.

About 2-3 weeks after surgery, the catheter is usually removed. Upon removal of the catheter, patients should be able to demonstrate Kegel exercises. There should also be a discussion with the patient about incontinence. Patients often need reassurance that this is expected, and they may need information on different incontinence products.

At three months after treatment, a follow-up visit should be planned to discuss how the patient is doing with incontinence. If possible, a referral for urodynamic assessment (where available) may be considered to assess options for bio-feedback training to help the patient regain control.

If the patient is still having trouble with incontinence problems at 12 months post-treatment, consider referral for an incontinence device (a pump that is inserted during day surgery).

7.2.3 Loss of Libido, Hot Flashes, Mood Swings

These symptoms are caused by testosterone reduction and occur during hormonal treatment, and possibly for months to years afterwards. Supportive care and or medications (see Appendix VII) may be considered.

7.2.4 Proctitis

Chronic irritation of the lower rectum occurs in about 10% percentage of prostate cancer patients treated with external radiation. The symptom of mild rectal bleeding usually develops within 6-12 months after radiation, due to vessel telangiectasia. It may last for years, usually improving with time. Proctitis may also cause discomfort during defecation or rectal urgency.

Any patient with persistent rectal bleeding needs full assessment including

colonoscopy by a gastroenterologist or surgeon. Once confirmed, radiation-induced proctitis can be treated symptomatically by modifying diet (to ensure avoidance of constipation) and with medications or procedures, listed below.

For patients with clinically significant symptoms of proctitis (rectal urgency, tenesmus, pain with bowel movements) treatment with either Anusol®- HC (*Hydrocortisone Acetate - Zinc Sulfate*) suppositories 1 PR q8h prn or Proctosone® or Proctosedyl® (*Hydrocortisone Acetate - Framycetin Sulfate - Cinchocaine HCL - Esculin*) suppositories 1 PR q8h prn, is recommended. If these do not provide adequate relief, Proctofoam™- HC (*Hydrocortisone Acetate - Pramoxine HCL*), Anugesic® - HC (*Pramoxine HCL - Hydrocortisone Acetate - Zinc Sulfate*), Xylocaine® (*Lidocaine HCL*) jelly 2%, all given PR q8h prn, or oral analgesics can be prescribed, in severe cases.

For bleeding occurring more than one year after radiation treatment, mesalamine (Salofalk®, Rowasa®) suppositories 1000mg PR for two weeks, repeated on a monthly basis, can be helpful. Occasionally, local therapy such as laser treatment is required for refractory bleeding requiring transfusion. Hyperbaric oxygen can also be helpful for recurrent bleeding. If life-threatening bleeding occurs, instillation of Formalin has also been shown to be effective to stop bleeding. In cases of complete, persistent incontinence, severe refractory rectal pain or fistula, defunctioning colostomy should be considered.

7.3 Other Resources

Some prostate cancer patients may benefit from involvement of the local palliative care service, for advanced symptom management expertise and end of life care when appropriate.

Referral to palliative care is available across the province, as illustrated in Figure 8.13.

Guidelines for the management of symptoms are under development by the *CCNS* Supportive Care Cancer Site Team. As these guidelines are completed, they are posted on the *Cancer Care Nova Scotia* website (www.cancercare.ns.ca). Current *CCNS* symptom management guidelines are:

- Management of Nausea & Vomiting (2004)
- Management of Cancer-Related Pain (2006)
- Management of Oral Complications from Cancer Therapy (2006)

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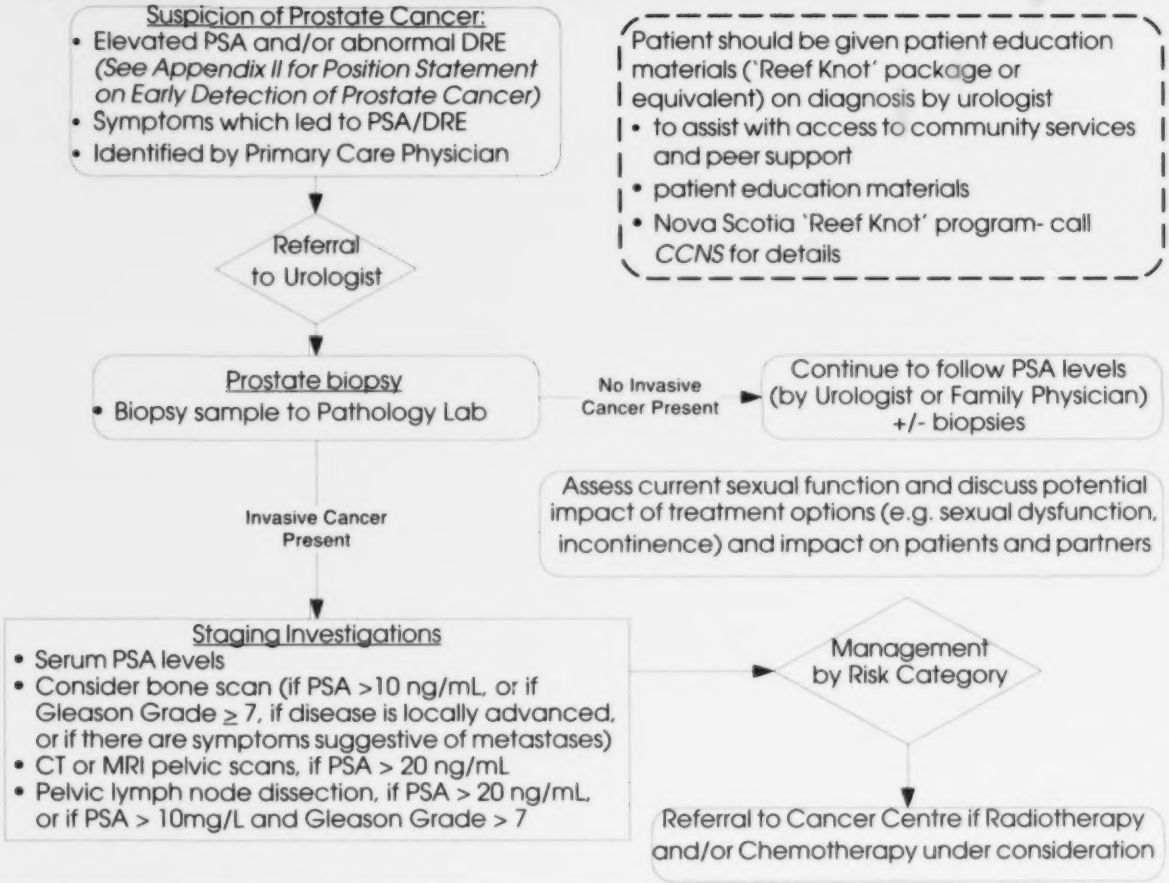
Part 8. Practice Pathways

8.1 Diagnosis and Referral of Prostate Cancer- Overview


Suspicion of Prostate Cancer:
• Elevated PSA and/or abnormal DRE (See Appendix II for Position Statement on Early Detection of Prostate Cancer)
• Symptoms which led to PSA/DRE
• Identified by Primary Care Physician
Patient should be given patient education materials ('Reef Knot' package or equivalent) on diagnosis by urologist
• to assist with access to community services and peer support
• patient education materials
• Nova Scotia 'Reef Knot' program- call CCNS for details
Referral to Urologist
Prostate biopsy
• Biopsy sample to Pathology Lab
No Invasive Cancer Present
Continue to follow PSA levels (by Urologist or Family Physician) +/- biopsies
Assess current sexual function and discuss potential impact of treatment options (e.g. sexual dysfunction, incontinence) and impact on patients and partners
Invasive Cancer Present
Staging Investigations
• Serum PSA levels
• Consider bone scan (if PSA >10 ng/mL, or if Gleason Grade ≥ 7, if disease is locally advanced, or if there are symptoms suggestive of metastases)
• CT or MRI pelvic scans, if PSA > 20 ng/mL
• Pelvic lymph node dissection, if PSA > 20 ng/mL, or if PSA > 10mg/L and Gleason Grade > 7
Management by Risk Category
Referral to Cancer Centre if Radiotherapy and/or Chemotherapy under consideration

Referral Information:

A letter of referral is the minimal requirement for a referral. A referral need not be delayed due to delays in scheduling tests or delayed reporting of tests

Local Urologist

- Refer as per usual practice within local community or health care district

QEII Health Sciences Centre:

- Faxed referrals to the QEII Cancer Care Program (CCP) Referrals Office at 902-473-6079 (tel. 902-473-5140 or 902-473-6098). It is preferred that referrals be accompanied by the CCP Referral form available upon request at the above phone numbers or available for downloading at www.cdha.nshealth.ca/physicianupdate

Cape Breton Cancer Centre:

- Direct referrals to the Referrals/Booking office at 902-567-7774 (fax 902-567-7911)

Urgent Referrals:

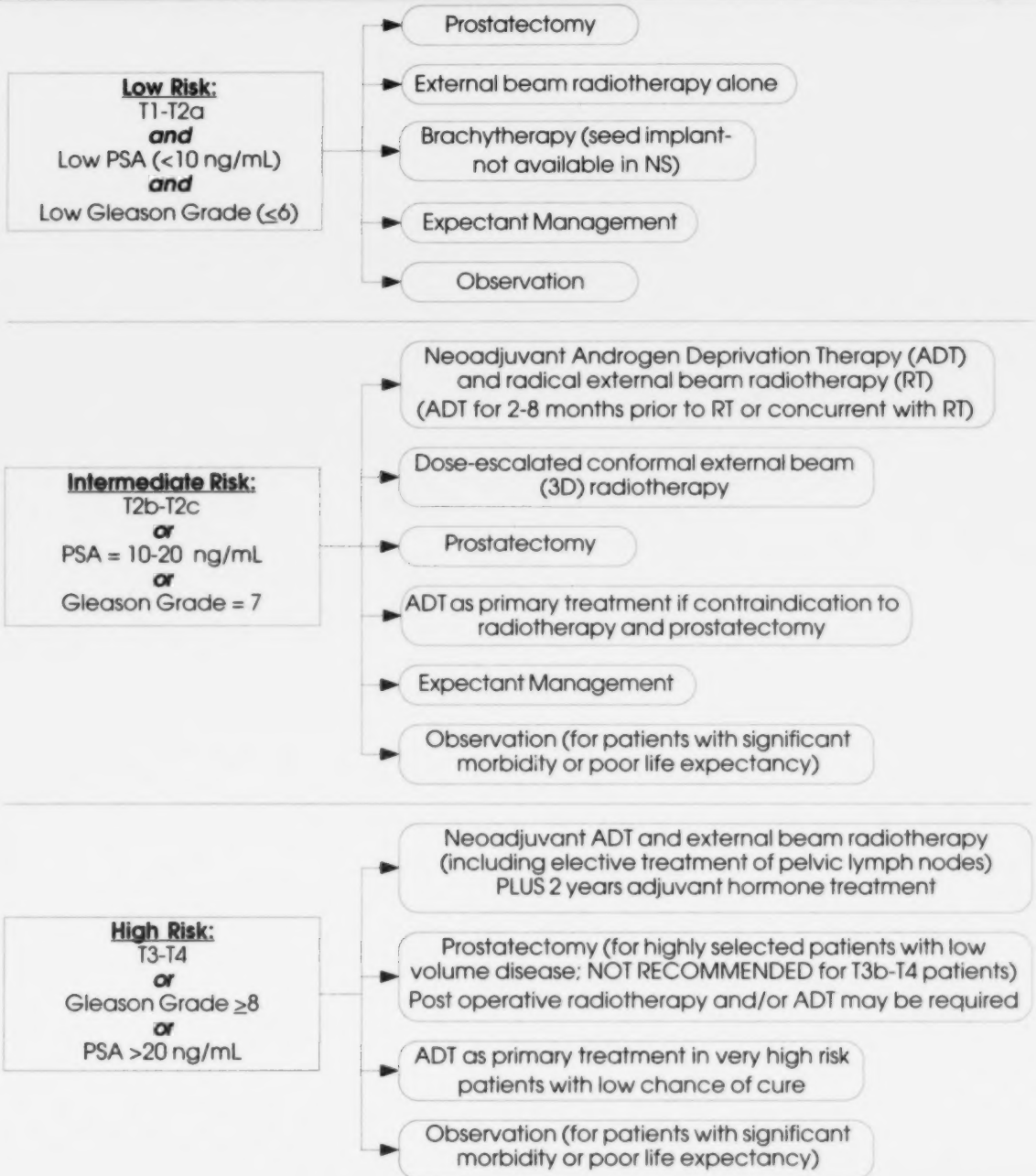
- For urgent or emergent referrals, in Halifax- page the appropriate specialist on call through the Locating service (902-473-2220); in Cape Breton- page the appropriate specialist on call through the Locating service (902-567-8000)

Referral Information:

- Letter of Referral*
- Laboratory Results*- CBC, PSA (including old results)
- Biopsy Pathology Reports
- Operative Reports (prostatectomy, orchiectomy, other)
- Diagnostic Imaging Reports (TURP, bone scans, chest X-ray, CT scans, other)

* *Specific information which is necessary for proper triage of referrals*

8.2 Initial Treatment Options for Prostate Cancer


Low Risk:
T1-T2a
and
Low PSA (<10 ng/mL)
and
Low Gleason Grade (≤6)
Prostatectomy
External beam radiotherapy alone
Brachytherapy (seed implant- not available in NS)
Expectant Management
Observation
Intermediate Risk:
T2b-T2c
or
PSA = 10-20 ng/mL
or
Gleason Grade = 7
Neoadjuvant Androgen Deprivation Therapy (ADT) and radical external beam radiotherapy (RT) (ADT for 2-8 months prior to RT or concurrent with RT)
Dose-escalated conformal external beam (3D) radiotherapy
Prostatectomy
ADT as primary treatment if contraindication to radiotherapy and prostatectomy
Expectant Management
Observation (for patients with significant morbidity or poor life expectancy)
High Risk:
T3-T4
or
Gleason Grade ≥8
or
PSA >20 ng/mL
Neoadjuvant ADT and external beam radiotherapy (including elective treatment of pelvic lymph nodes) PLUS 2 years adjuvant hormone treatment
Prostatectomy (for highly selected patients with low volume disease; NOT RECOMMENDED for T3b-T4 patients) Post operative radiotherapy and/or ADT may be required
ADT as primary treatment in very high risk patients with low chance of cure
Observation (for patients with significant morbidity or poor life expectancy)

8.3 Observation

- Observation consists of medical follow up where it is unlikely that the patient will be treated with radiation therapy or surgery for cure due to a limited life expectancy or severe medical co-morbidities. Treatment at symptomatic progression will likely consist of ADT with additional interventions given with the intent of improving impairments in prostate cancer-specific health-related quality of life.

8.4 Expectant Management

- Expectant management involves actively monitoring the course of disease with the expectation to intervene if the cancer progresses or if symptoms become imminent
- Patients with clinically localized cancers that are candidates for definitive treatment and choose expectant management should have regular follow up
  - DRE and PSA every six months
  - Needle biopsy of the prostate may be repeated within 6 mo of diagnosis if initial biopsy was < 10 cores or assessment discordant (eg, palpable tumour contralateral to side of positive biopsy)
  - Needle biopsy should be performed within 18 months if > 10 cores obtained initially, then periodically
- A repeat biopsy may be indicated for any sign of disease progression by exam or markers

8.5 ADT (Androgen Deprivation Therapy - Hormonal Regimens)

The choice of initial orchiectomy or androgen deprivation (hormonal) agent(s) for any individual patient will depend on many factors.

- Combined Androgen Blockade (CAB- LHRH agonist plus non-steroidal antiandrogen agent) is not routinely indicated
- Monotherapy with nonsteroidal antiandrogens is not routinely indicated
- After initial failure of ADT, secondary hormonal manipulation should be tried (eg. addition of a non-steroidal antiandrogen or discontinuation of non-steroidal antiandrogen if already on)
- Other hormonal manipulations, such as ketoconazole or estrogens may be tried. Some phase II trials show a decline in PSA. There are no randomized data to support any survival advantage

OPTIONS:

1. Orchiectomy

The testicles are surgically removed. The procedure is done as an outpatient, usually done under local anesthetic. Surgical castration (orchiectomy) is permanent.

2. LHRH Agonists

Goserilin (Zoladex®) 3.6 mg SC Depot q28d OR 10.8 mg SC Depot q84d

Leuprolide (Lupron®-IM, Eligard®-SC) 7.5 mg q28d OR 22.5 mg q84d (3mo) IM/SC Depot OR 30 mg q112d (4 mo)/ 45 mg q168d (6mo) SC Depot

Buserilin (Suprefact®) 6.3 mg SC Depot q56d OR 9.45 mg IM Depot q120d

Note: Due to an initial rise in testosterone levels, patients should be given a non-steroidal antiandrogen (see below) for 2-4 weeks at the same time as their first LHRH agonist dose

3. Non-steroidal Antiandrogen Agents

Flutamide (Euflex®) 250 mg PO TID

Bicalutamide (Casodex®) 50 mg PO daily, up to 150 mg PO daily to TID

Nilutamide (Anandron®) 50 mg PO BID or TID

4. Other Hormonal Treatments

Cyproterone (Androcur®) 50-100 mg PO BID or TID

Megestrol (Megace®) 80-160 mg PO daily

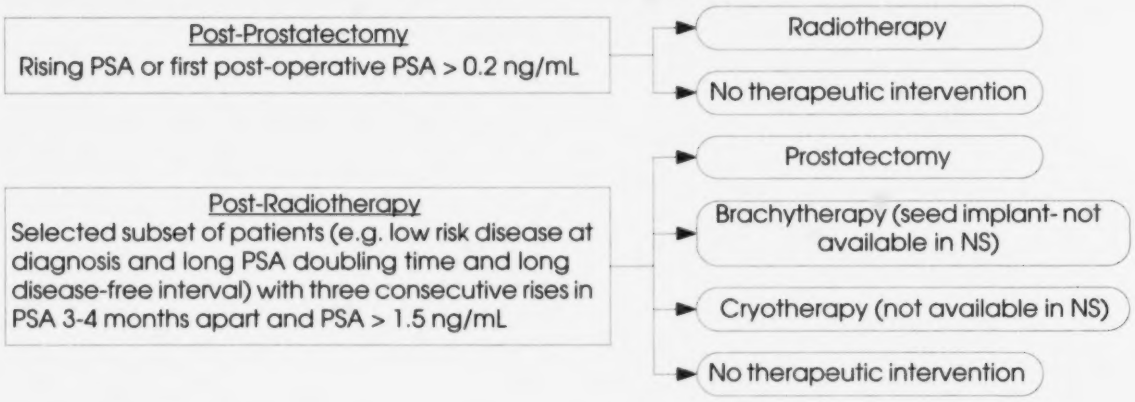
Ketoconazole (Nizoral®) 400 mg PO TID (+/- Hydrocortisone 20 mg qAM & 10 mg qPM)

Estrogens- e.g. Diethylstilbestrol 1 mg PO Daily

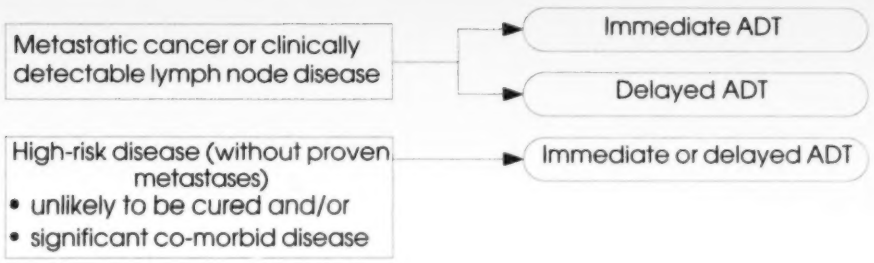
8.6 Post-Prostatectomy Management

Post-operative PSA Undetectable or PSA < 0.2 ng/mL
pT2, pT0 NX,N0 M0 negative margin
No therapeutic interventions, standard follow-up management
pT2 (positive margin), pT3a NX,N0 M0
No therapeutic interventions, standard follow-up management
Radiation Therapy (+/- ADT)
pT3b NX,N0 M0
ADT alone
Radiation Therapy (+/- ADT)
No therapeutic interventions, standard follow-up management
Assess effect of treatment(s) on patient function (esp. incontinence & sexual dys-function) and psychosocial distress. Manage symptom(s) and distress as appropriate
pT4 NX,N0 M0
Radiation Therapy (+/- ADT)
ADT alone
No therapeutic interventions
pTX N+ M0
ADT alone
No therapeutic interventions, standard follow-up management
Post-operative PSA Detectable PSA ≥ 0.2 ng/mL
See Salvage Therapy

8.7 Salvage Therapy

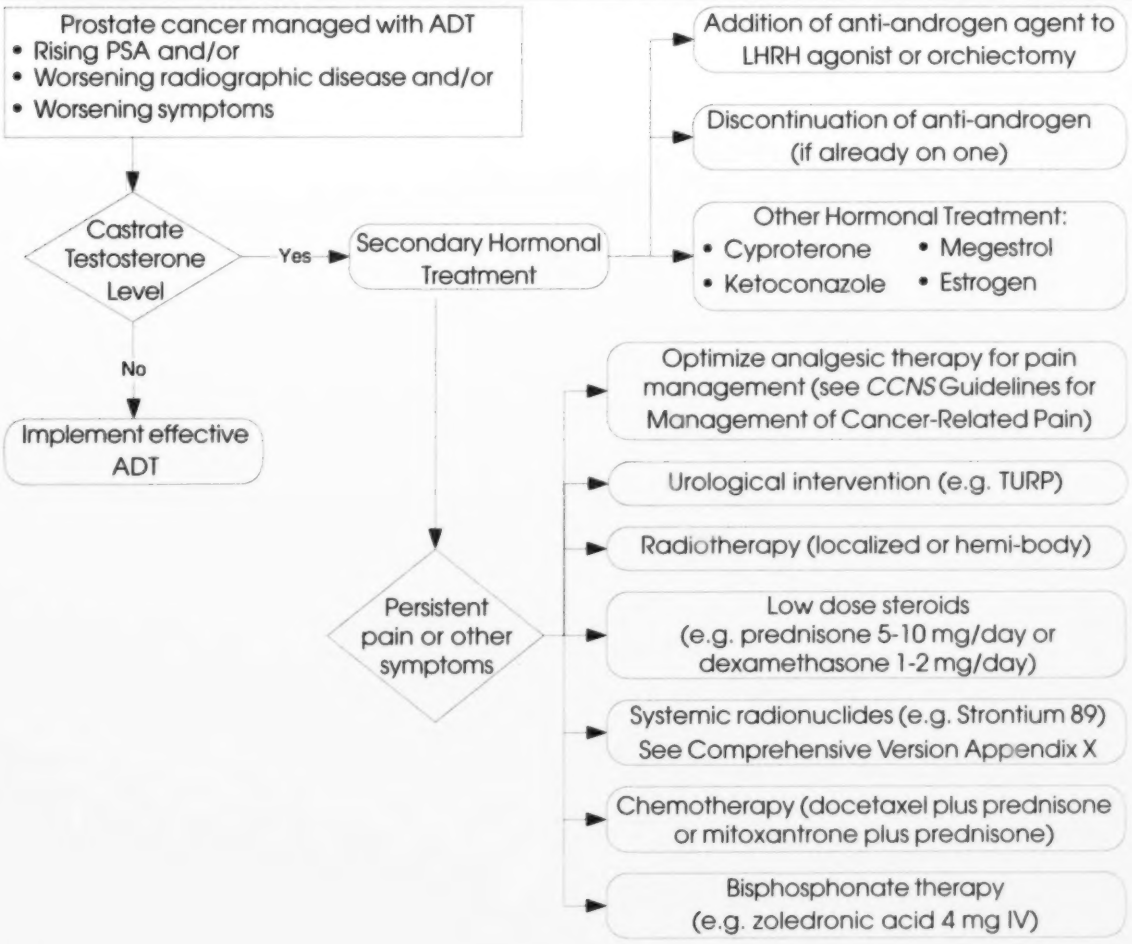

Post-Prostatectomy
Rising PSA or first post-operative PSA > 0.2 ng/mL
Radiotherapy
No therapeutic intervention
Post-Radiotherapy
Selected subset of patients (e.g. low risk disease at diagnosis and long PSA doubling time and long disease-free interval) with three consecutive rises in PSA 3-4 months apart and PSA > 1.5 ng/mL
Prostatectomy
Brachytherapy (seed implant- not available in NS)
Cryotherapy (not available in NS)
No therapeutic intervention

8.8 Metastatic and Incurable Prostate Cancer


Metastatic cancer or clinically detectable lymph node disease
Immediate ADT
Delayed ADT
High-risk disease (without proven metastases)
• unlikely to be cured and/or
• significant co-morbid disease
Immediate or delayed ADT

Consider referral to Palliative Care service (see page 29) and/or provincial home care service

8.9 Hormone Refractory Prostate Cancer


Prostate cancer managed with ADT
• Rising PSA and/or
• Worsening radiographic disease and/or
• Worsening symptoms
Castrate Testosterone Level
Yes
Secondary Hormonal Treatment
Addition of anti-androgen agent to LHRH agonist or orchiectomy
Discontinuation of anti-androgen (if already on one)
Other Hormonal Treatment:
• Cyproterone
• Megestrol
• Ketoconazole
• Estrogen
No
Implement effective ADT
Persistent pain or other symptoms
Optimize analgesic therapy for pain management (see CCNS Guidelines for Management of Cancer-Related Pain)
Urological intervention (e.g. TURP)
Radiotherapy (localized or hemi-body)
Low dose steroids (e.g. prednisone 5-10 mg/day or dexamethasone 1-2 mg/day)
Systemic radionuclides (e.g. Strontium 89) See Comprehensive Version Appendix X
Chemotherapy (docetaxel plus prednisone or mitoxantrone plus prednisone)
Bisphosphonate therapy (e.g. zoledronic acid 4 mg IV)

8.10 Management of Sexual Dysfunction

Pre-treatment assessment for normal sexual function

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Initiate post-operative/post-treatment discussions (6-12 weeks after treatment):
- Consider institution of oral agents (sildenafil (Viagara®), tadalafil (Cialis®), vardenafil (Levitra®)) to conserve penile health
  - Urologist/radiation oncologist

↓

At 3-12 months post-treatment:
- Assess efficacy of oral agents and need for sexual function
- If ineffective, consider penile injection therapy
  - Erectile Dysfunction clinic or urologist/radiation oncologist
- Consider couple counselling as appropriate

↓

Reassess at 12 months:
- Sexual function, distress issues

8.11 Management of Incontinence

Pre-treatment visit:
- Assessment of bladder function
- Instruction on Kegel exercises
- Training on incontinence products
- Discussion with patient about incontinence

↓

2-3 weeks postop (at time of catheter removal):
- Discussion with patient about incontinence
- Patient demonstration of Kegel exercises

↓

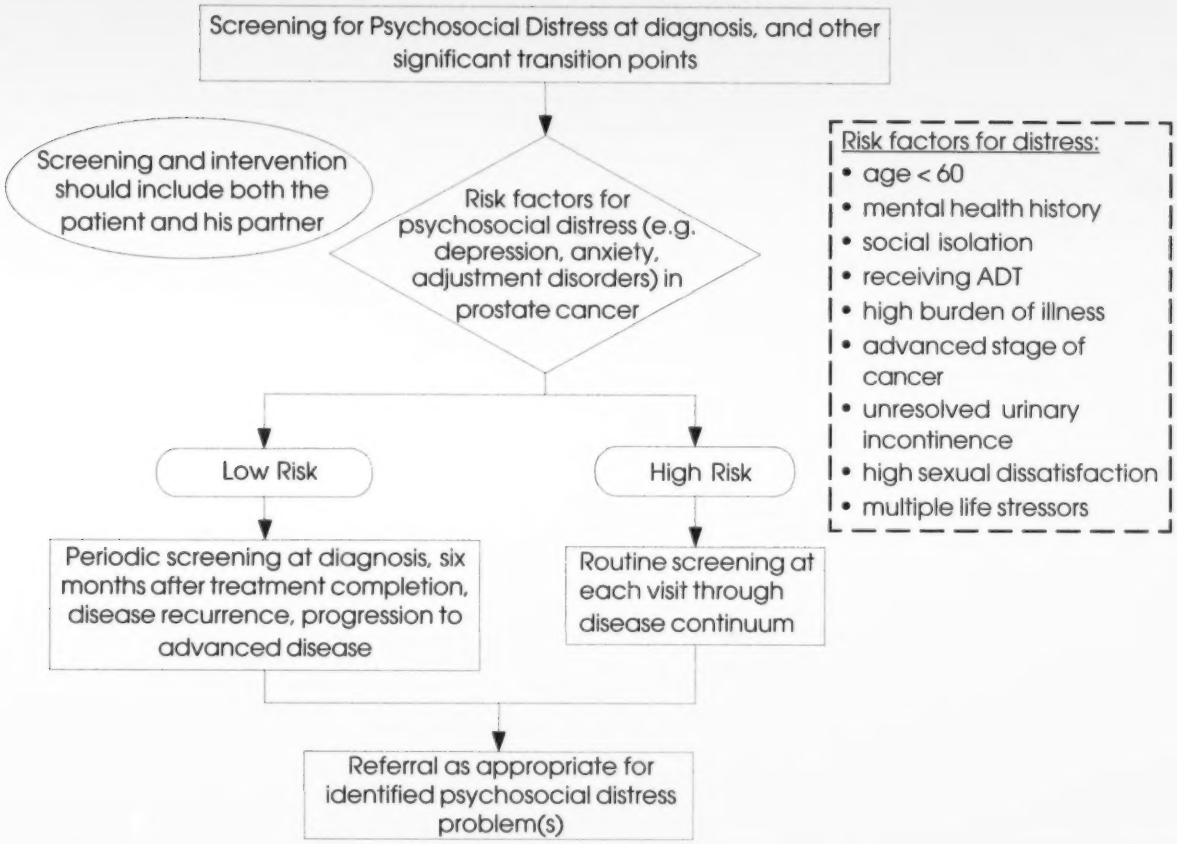
Three months post treatment:
- Discussion with patient about any incontinence
- Referral for Urodynamic studies, if necessary

↓

One year post treatment:
- Reassess level of continence, consider incontinence device if necessary

See Management of Psychosocial Issues (8.12)

8.12 Management of Psychosocial Issues


Screening for Psychosocial Distress at diagnosis, and other significant transition points
Screening and intervention should include both the patient and his partner
Risk factors for psychosocial distress (e.g. depression, anxiety, adjustment disorders) in prostate cancer
Risk factors for distress:
• age < 60
• mental health history
• social isolation
• receiving ADT
• high burden of illness
• advanced stage of cancer
• unresolved urinary incontinence
• high sexual dissatisfaction
• multiple life stressors
Low Risk
High Risk
Periodic screening at diagnosis, six months after treatment completion, disease recurrence, progression to advanced disease
Routine screening at each visit through disease continuum
Referral as appropriate for identified psychosocial distress problem(s)

8.13 Management of Pain and Other Symptoms

Referral of a cancer patient who needs help with pain or symptom management, or for palliative care

To The Attending Oncology Team:
- See page 23

To The Cancer Patient Navigator:
- 1-866-524-1234 from anywhere in Nova Scotia

To The District Palliative Care/Supportive Care Service:

South Shore Health:
- 902-634-7369 or 902-354-3436

South West Health:
- 902-742-3542 Ext. 414.

Annapolis Valley Health:
- 902-678-7381 Ext. 2270

Colchester East Hants Health Authority:
- 902-893-5554 Ext. 2306

Cumberland Health Authority:
- 902-667-5400 Ext. 6373

Pictou County Health:
- 902-752-7600 Ext. 4190

Guysborough Antigonish Strait Health Authority:
- 902-867-4296 or 902-867-4436

Cape Breton District Health Authority:
- 902-567-7846

Capital Health Cancer Care Program:
- 902-473-3119

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1278 Tower Road
5th floor Bethune Building
Halifax, Nova Scotia B3H 2Y9

Phone: 902-473-4645
Toll free: 1-866-599-2267
Fax: 902-473-4631

Email: info@ccns.nshealth.ca
www.cancercare.ns.ca